M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: March 18, 1999

To: Dockets Management Branch (HFA-305)

From: Ted Sherwood
Management Analyst
Office of Generic Drugs

Subject: Presentation Regarding Human Generic Drugs to Docket 90S-0308

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation: A Case Study for SUPAC IR

Presented for: AAPS

Date Presented: March 15, 1999

Presented by: Liang-Lii Huang, Ph.D.

Number of Pages: 12

Edward M Sherwood

Attachment

90S-0308

M632 b8

A CASE STUDY for SUPAC IR

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Review Chemist
FDA, Office of Generic Drugs

Background

ABC Company

Manufacturing Site Changes

- Manufacturing site: New Jersey
- New manufacturing site : Puerto Rico

GMP Compliance

- The Puerto Rico facility had a satisfactory cGMP inspection within the last two years.

Background

ABC Company

Batch Size Changes

- reduced: 500 kg → 280 kg

Process Changes

- hand screening → automatic screening process

Equipment Changes

- P-K v-shell → bin blender
- Fette → Manesty tablet press

ABC Company's
Proposed Submission and Supporting Documentation

- Supplement - Changes Being Effected (CBE) in 30 days
- One batch of drug product release data
- One batch on accelerated & long term stability (based on significant body of data available)
- Case B multi-point dissolution profile
- Updated batch records
- Name and address of the new facility
- Stability data on the first three production batches manufactured at the new facility will be provided in annual report.

Summary

filing requirements & documentation

Level 3 Site changes: CBE supplement

Supporting documents:

- application/ compendial release requirements
- location of new site & updated batch records
- case B dissolution profile
- one batch /3 months accelerated stability data in the supplement (based on significant body of data available)
- one batch on long term stability/ annual report

Summary

filing requirements & documentation

Level 1 batch size changes: Annual report

Supporting documents:

- application/ compendial release requirements
- notification of change & submission of updated batch records in annual report
- one batch on long term stability data in the annual report

Summary

filing requirements and documentation

Level 2 process changes: CBE supplement

Supporting documents:

- application/ compendial release requirements
- notification of changes & submission of updated batch records
- one batch on long term stability (long term stability data in annual report)
- case B dissolution profile

Summary

filing requirements & documentation

Level 1 equipment changes: Annual report

Supporting documents:

- application/ compendial release requirements
- notification of changes & submission of updated batch records
- one batch on long term stability (long term stability data in annual report)
- dissolution: none beyond application/ compendial release requirements

Issues

- Which individual change would be used for SUPAC filing and documentation in this case ?
- Missing information ?
- Equipment changes ? (use manufacturing equipment addendum)

Conclusion

- The ABC company's proposal is considered acceptable.
- Among the proposed changes, the most restrictive change has generally been accepted as the basis of the decision for filing & documentation. In this case study, Level 3 site change is the answer.
- Therefore, this case would be submitted as a CBE supplement.

Conclusion

Test documentation would include:

- application/ compendial release requirements
- location of new site & submission of updated batch records
- case B dissolution profile
- one batch /3 months accelerated stability data in the supplement (based on significant body of data available)
- one batch on long term stability/ annual report

Conclusion

- Changes in batch size are not based on the size of granulation but on the number of units produced.
- The SUPAC IR guidance is not applicable to scale-down below 100,000 units.
- SUPAC IR does not cover multiple changes. We recommend that CDER be contacted if multiple changes are to be made.